(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Veröffentlichungsnummer:
(11) Publication number: 0 726 749
(11) Numéro de publication:

Internationale Anmeldung veræffentlicht durch die Weltorganisation fßr geistiges Eigentum unter der Nummer:

WO 95/12371 (art.158 des EP*f*).

International application published by the World Intellectual Property Organisation under number:

WO 95/12371 (art.158 of the EPC).

Demande internationale publieà par l'Organisation Mondiale de la Propriàtà sous le numàro:

WO 95/12371 (art.158 de la CBE).

European Patent Office

SUPPLEMENTARY EUROPEAN SEARCH REPORT

Application Number
EP 95 90 1740

DOCUMENTS CONSIDERED TO BE RELEVANT

	Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
2	X	EP 0 341 007 A (PROJECT HEAR ;MATRIX PHARMA (US)) 8 November 1989 (1989-11-08) * page 3, line 18 - line 25; claims * ---	1,2	A61L25/00 A61L15/44 A61L15/64 A61F13/02
2	X	US 4 006 220 A (GOTTLIEB SHELDON K) 1 February 1977 (1977-02-01) * claims * ---	1,2	
2	X	US 4 061 731 A (GOTTLIEB SHELDON K) 6 December 1977 (1977-12-06) * claims * ---	1,2	
2	X	DATABASE WPI Section Ch, Week 197937 Derwent Publications Ltd., London, GB; Class A96, AN 1979-66949B XP002128893 & JP 54 098091 A (UNITIKA LTD), 2 August 1979 (1979-08-02) * abstract * ---	1,2	
2	X	DATABASE WPI Section Ch, Week 198029 Derwent Publications Ltd., London, GB; Class B04, AN 1980-51199C XP002128894 & SU 700 129 A (KIEV HAEMATOLOGY), 30 November 1979 (1979-11-30) * abstract * ---	1,2	TECHNICAL FIELDS SEARCHED (Int.Cl.6) A61L A61F
2	A	EP 0 365 705 A (TS PROBLEMNA LAB KRYOBIOLOGIA) 2 May 1990 (1990-05-02) * claims; examples * ---	1-9	
2	A	US 4 637 815 A (LEMOLE GERALD M) 20 January 1987 (1987-01-20) * claims * ---	1-9	
		-/--		

1 The supplementary search report has been based on the last set of claims valid and available at the start of the search.

Place of search	Date of completion of the search	Examiner
THE HAGUE	27 January 2000	ESPINOSA, M

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C04)

European Patent Office

SUPPLEMENTARY EUROPEAN SEARCH REPORT

Application Number
EP 95 90 1740

DOCUMENTS CONSIDERED TO BE RELEVANT

	Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
2	A	WO 93 06855 A (NOVONORDISK AS) 15 April 1993 (1993-04-15) ---		
2	A	WO 90 13320 A (FERROSAN AS) 15 November 1990 (1990-11-15) -----		

TECHNICAL FIELDS SEARCHED (Int.Cl.6)

1 The supplementary search report has been based on the last set of claims valid and available at the start of the search.

Place of search	Date of completion of the search	Examiner
THE HAGUE	27 January 2000	ESPINOSA, M

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C04)

Claims:

1. A hemostatic patch adapted for rapidly and without pre-moistening arresting bleeding from a lesion on a parenchymal organ, in the form of a dry sterile storage stable fibrinogen-free flexible sheet of a biodegradable matrix containing a hemostatic agent on one face only thereof, which hemostatic agent comprises an amount of thrombin, optionally bovine thrombin, effective to promote accelerated hemostasis and an amount of epsilon aminocaproic acid effective to inhibit fibrinolysis and to accelerate the activation of the thrombin when the patch is applied to the bleeding lesion;

optionally said patch containing one or more of a source of calcium ions, RGD peptide, RGDS peptide, protamine sulfate and buffer.

2. A hemostatic patch according to claim 1, wherein the biodegradable matrix is:

(a) a foam, optionally an absorbable gelatin foam; or

(b) selected from absorbable gelatin, calcium alginate, calcium/sodium alginate, collagen and oxidized regenerated cellulose.

3. A hemostatic patch according to claim 1 or claim 2, wherein:

(a) the epsilon aminocaproic acid is present in an amount from about 10-100mg/cm^2 of the wound-contacting

surface of the matrix, e.g. 60-70mg/cm^2 of the wound-contacting surface of the matrix; and/or

(b) the thrombin is present in an amount between 1-4 IU/cm^2 of the wound-contacting surface of the matrix; and/or

(c) calcium ions are present in an amount equivalent to 25-150 micrograms $CaCl_2$/cm^2 of the wound-contacting surface of the matrix.

4. A dry sterile storage stable fibrogen-free hemostatic patch comprising a biodegradable matrix containing a hemostasis-promoting amount of thrombin, optionally bovine thrombin, and an amount of a compound which is effective to raise the pH of fluid on a bleeding wound surface onto which the hemostatic patch is applied to a value in the range of 7.0-9.0, e.g. 7.62-8.02, inclusive, and which is thereby effective to accelerate the activation of the thrombin and thus accelerate clot formation at the interface between the wound surface and the hemostatic patch.

5. A hemostatic patch according to claim 4, wherein the thrombin-activating compound is epsilon aminocaproic acid.

6. A hemostatic patch according to claim 4 or claim 5 and further defined by any specific feature(s) of any one or more of claims 2 and 3.

7. A hemostatic patch according to claim 4, wherein the biodegradable matrix is a flexible sheet of an absorbable gelatin foam, wherein the patch

optionally contains one or more of a source of RGD peptide, RGDS peptide, protamine sulfate and buffer; wherein epsilon aminocaproic acid is present therein in an amount between 60-70mg/cm^2 of the wound-contacting surface of the matrix; wherein the thrombin is present therein in an amount between 1-4 IU/cm^2 of the wound-contacting surface of the matrix; and wherein calcium ions are present in an amount equivalent to between 25-150 micrograms of $CaCl_2/CM^2$ of the wound-contacting surface of the matrix.

8. A sterile package containing a hemostatic patch according to any one of claims 1 to 7.

9. The use of a dry sterile storage stable fibrinogen-free biodegradable matrix containing a hemostatic agent, which hemostatic agent comprises an amount of thrombin, optionally bovine thrombin, effective to promote accelerated hemostasis and an amount of epsilon aminocaproic acid effective to inhibit fibrinolysis and to accelerate the activation of the thrombin, in the manufacture of a medicament patch.